

CLAIMS:

1. An isolated gene comprising introns having a sequence of:
 - (i) nucleotides 1018 to 1046 of SEQ ID NO: 1; and
 - (ii) nucleotides 1676 to 1718 of SEQ ID NO: 1.
2. An isolated polynucleotide complementary to a messenger RNA transcribed from the gene of claim 1 or 2.
3. A polynucleotide selected from the group consisting of:
 - g) a polynucleotide comprising SEQ ID NO: 2;
 - h) a polynucleotide comprising SEQ ID NO: 52;
 - i) a polynucleotide comprising SEQ ID NO: 54;
 - j) a polynucleotide comprising SEQ ID NO: 55;
 - k) an allelic variant of any of (a) to (d) comprising at least one polymorphic variation compared to any of (a) to (d) respectively, wherein said polymorphic variation is selected from the group consisting of UBP8rp-related biallelic markers Nos. 1 to 96 shown below.
 - l) a polynucleotide complementary to any of (a) to (e).

Biallelic marker No.	Position on SEQ ID NO: 1	Alternative nucleotides
1	1199	A/G
2	1262	C/T
3	1426	C/G
4	1444	G/T
5	1487	A/G
6	1490	A/G
7	1505	G/T
8	1518	C/T
9	1554	C/T
10	1630	A/G
11	1638	A/T
12	1680	A/G
13	1895	A/G
14	2180	A/G
15	2449	A/T
16	2721	G/T
17	3127	A/G
18	3137	C/T
19	3138	A/G
20	3183	A/G
21	3222	C/G
22	3269	C/T
23	3445	C/T

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Biallelic marker No.	Position on SEQ ID NO: 1	Alternative nucleotides
24	3470	A/G
25	3915	C/T
26	3973	A/C
27	4254	A/G
28	4472	A/T
29	4660	C/T
30	4770	A/G
31	4919	A/G
32	4973	C/T
33	5063	C/T
34	5065	G/T
35	5079	C/T
36	5080	C/T
37	5088	C/G
38	5090	C/T
39	5407	C/T
40	5466	A/G
41	5520	C/T
42	829	A/G
43	856	A/G
44	902	insertion of G
45	908	insertion of A
46	972	A/G
47	975	A/G
48	1006	C/T
49	1018	A/G
50	1048	A/C
51	1056	C/T
52	1069	G/T
53	1073	A/G
54	1079	A/G
55	1108	A/G
56	1154	A/G
57	1181	A/G
58	1236	A/G
59	1263	A/G
60	1274	A/G
61	1319	G/T
62	1334	A/G
63	1444	G/T
64	1466	C/T
65	1489	A/G
66	1508	C/T
67	1521	G/T
68	1543	A/G

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Biallelic marker No.	Position on SEQ ID NO: 1	Alternative nucleotides
69	1687	A/C
70	1707	deletion of C
71	1728	A/G
72	1742	C/T
73	1810	C/T
74	1813	A/C
75	1841	C/T
76	1874	C/G
77	1875	A/G
78	1890	A/C
79	1907	A/G
80	1909	C/T
81	1921	A/C
82	1922	A/G
83	1957	A/G
84	1959	A/G
85	1976	C/T
86	1992	C/T
87	1993	C/T
88	2096	C/G
89	2135	A/G
90	2192	A/G
91	2230	C/G
92	2275	C/T
93	2314	A/G
94	2370	A/C
95	2375	A/T
96	2525	C/T

4. An isolated polypeptide encoded by the polynucleotide of any of claims 1 to 3.
5. The polypeptide of claim 4, wherein said polypeptide is selected from the group consisting of:
 - 5 a) a polypeptide comprising SEQ ID NO:3;
 - b) a polypeptide comprising a span of at least 470 amino acids of SEQ ID NO: 3;
 - c) a polypeptide comprising a span of at least 15 amino acids of SEQ ID NO: 3, wherein said span falls within amino acids 467 to 482 of SEQ ID NO: 3;
 - 10 d) an allelic variant of any of (a) to (c) comprising at least one polymorphic variation compared to any of (a) to (c) respectively, wherein said polymorphic variation is encoded by a codon comprising a UBP8rp-related biallelic marker of the table set forth in claim 3;

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- 5 e) a mutein of any of (a) to (c), wherein the amino acid sequence has at least 95%, 96%, 97%, 98% or 99% identity to at least one of the sequences in (a) to (c);
- f) a mutein of any of (a) to (c) which is encoded by a nucleic acid which hybridizes to the complement of a DNA sequence encoding any of (a) to (c) under highly stringent conditions; and
- g) a mutein of any of (a) to (c) wherein any changes in the amino acid sequence are conservative amino acid substitutions of the amino acid sequences in (a) to (c).
6. The polypeptide of claim 4, wherein said polypeptide is selected from the group consisting of:
- 10 a) a polypeptide comprising SEQ ID NO:53;
- b) a polypeptide comprising a span of at least 470 amino acids of SEQ ID NO: 53;
- c) a polypeptide comprising a span of at least 15 amino acids of SEQ ID NO: 53, wherein said span falls within amino acids 467 to 485 of SEQ ID NO: 3;
- 15 d) a mutein of any of (a) to (c), wherein the amino acid sequence has at least 95%, 96%, 97%, 98% or 99% identity to at least one of the sequences in (a) to (c);
- e) a mutein of any of (a) to (c) which is encoded by a nucleic acid which hybridizes to the complement of a DNA sequence encoding any of (a) to (c) under highly stringent conditions; and
- 20 f) a mutein of any of (a) to (c) wherein any changes in the amino acid sequence are conservative amino acid substitutions of the amino acid sequences in (a) to (c).
7. The polypeptide of claim 4, wherein said polypeptide is selected from the group consisting of:
- 25 a) a polypeptide comprising SEQ ID NO:56;
- b) a polypeptide comprising a span of at least 270 amino acids of SEQ ID NO: 56;
- c) a polypeptide comprising a span of at least 15 amino acids of SEQ ID NO: 56, wherein said span comprises amino acids 266 and 267 of SEQ ID NO: 56;
- 30 d) a mutein of any of (a) to (c), wherein the amino acid sequence has at least 95%, 96%, 97%, 98% or 99% identity to at least one of the sequences in (a) to (c);
- e) a mutein of any of (a) to (c) which is encoded by a nucleic acid which hybridizes to the complement of a DNA sequence encoding any of (a) to (c) under highly stringent conditions; and
- f) a mutein of any of (a) to (c) wherein any changes in the amino acid sequence are conservative amino acid substitutions of the amino acid sequences in (a) to (c).
8. An expression vector comprising the gene of claim 1 or 2.
- 35 9. An expression vector comprising the polynucleotide of claim 3 or 4.

10. The expression vector of claim 8 or 9, wherein said polynucleotide encodes the polypeptide of any of claim 5 to 7.
11. The expression vector of any of claim 8 to 10, wherein said vector is a gene therapy vector.
- 5 12. A host cell comprising the expression vector of any of claims 8 to 10.
13. A method of making a polypeptide, said method comprising the steps of culturing a host cell according to claim 12 under conditions suitable for the production of a polypeptide of claim 4 or 5 within said host cell.
14. The method of claim 13, further comprising the step of purifying said polypeptide from the culture.
- 10 15. The method of claim 14, further comprising the step of formulating said polypeptide into a pharmaceutical composition.
16. An antibody that specifically binds to the polypeptide of claim 4.
17. Use of a polypeptide of any of claim 4 to 7 as a target for screening for natural binding partners.
- 15 18. Use of the polypeptide of any of claim 4 to 7 as a target for screening candidate modulators.
19. The use of claim 18, wherein said candidate modulator is selected from the group consisting of a natural ligand, a small molecule, an aptamer, an antisense mRNA, a small interfering RNA and an antibody.
- 20 20. The use of claim 18 or 19, wherein said modulator is a candidate drug for the treatment of a chronic inflammatory disease.
21. The use of any of claims 18 to 20, wherein the activity of said polypeptide of any of claims 4 to 7 is assessed by measuring the de-ubiquitinating activity of UBP8 in the presence of said polypeptide of any of claim 4 to 7.
- 25 22. Use of a modulator of a polypeptide of any of claim 4 to 7 for preparing a medicament for the treatment of a chronic inflammatory disease.
23. The use of claim 22, wherein said modulator is used in combination with a known drug for said chronic inflammatory disease.
- 30 24. The use of any of claims 20 to 23, wherein said chronic inflammatory disease is psoriasis.

25. The use of any of claims 20 to 24, wherein said candidate modulator is an UBP8rp antagonist.
26. A method of assessing the efficiency of a modulator of a polypeptide of any of claim 4 to 7 for the treatment of psoriasis, said method comprising administering said modulator to an animal model for psoriasis; wherein a determination that said modulator ameliorates a representative characteristic of psoriasis in said animal model indicates that said modulator is a drug for the treatment of psoriasis.
27. The method of claim 26, wherein said representative characteristic is a Psoriasis Area and Severity Index score.
28. The method of claim 27, wherein a 75% or greater improvement in Psoriasis Area and Severity Index scores (PASI 75) indicates that said modulator is a drug for the treatment of psoriasis.
29. The method of any of claims 26 to 38, wherein said animal model is a SCID-hu Mouse.
30. Use of at least one UBP8rp-related biallelic marker for determining whether there is a significant association between said biallelic marker and a chronic inflammatory disease, wherein said UBP8rp-related biallelic marker is selected from the group consisting of biallelic markers Nos. 1, 2, 4, 6, 7, 10, 12-19, 21-30, 31-35 and 37-96 of the table set forth in claim 3.
31. The use of claim 30, wherein said chronic inflammatory disease is psoriasis.
32. Use of at least one UBP8rp-related biallelic marker selected from the group consisting of biallelic markers Nos. 1, 2, 4, 6, 7, 10, 12-19, 21-30, 31-35 and 37-96 of the table set forth in claim 3 for diagnosing whether an individual suffers from or is at risk of suffering from a chronic inflammatory disease,
33. The use according to claim 32, wherein the presence of allele A9 in said individual indicates that said individual suffers from or is at risk of suffering from said chronic inflammatory disease.
34. The use of claim 32 or 33, wherein said chronic inflammatory disease is psoriasis.
35. A method of genotyping comprising the steps of:
- a) isolating a nucleic acid from a biological sample; and
 - b) detecting the nucleotide present at one or more of the UBP8rp-related biallelic markers selected from the group consisting of biallelic markers Nos. 1, 2, 4, 6, 7, 10, 12-19, 21-30, 31-35 and 37-96 of the table set forth in claim 3.

36. The method of claim 35, wherein said biological sample is derived from a single individual.
37. The method of claim 36, wherein the identity of the nucleotides at said biallelic marker is determined for both copies of said biallelic marker present in said individual's genome.
- 5 38. The method of any of claims 35 to 37, wherein said determining is performed by a microsequencing assay.
39. The method of any of claims 35 to 38, further comprising amplifying a portion of a sequence comprising the biallelic marker prior to said determining step.
40. The method of claim 39, wherein said amplifying is performed by PCR.
- 10 41. The method of any of claims 35 to 40, further comprising the step of correlating the result of the genotyping steps with a risk of suffering from a chronic inflammatory disease.
42. The method of any of claims 36 to 41, wherein the presence of allele A9 in said individual indicates that said individual suffers from or is at risk of suffering from said chronic inflammatory disease.
- 15 43. The method of claim 42, wherein said chronic inflammatory disease is psoriasis.